122804
Shaughnessey No.

11/5/1985

DATA EVALUATION REPORT

ECOLOGICAL EFFECTS BRANCH

1. CHEMICAL: Affirm
   Sha. No: 122804

2. TEST MATERIAL: Avermection B_1, Avermectin B_{1a} Standard and 4 photodegradates.

3. STUDY/ACTION TYPE: 48-hour LC_{50} with Daphnia magna

4. STUDY ID: Author: Naimie, Hussein, Susan Anton, and Larry Kaelin
   Title: Results of Daphnid Bioassay of MK-0936, Avermectin B_{1a} Standard, Polar and Nonpolar Metabolites from a Water Photolysis Reaction of Avermectin B_{1a} Standard.
   Laboratory: Merck, Sharp and Dohme Research Laboratory
   Study No./Date: Appendix 2 of Acc. No. 258746 / July, 1985
   Study submitted to EPA by: Merck, Sharp and Dohme Laboratories
   Acc. No: 258746

5. REVIEWED BY: Daniel Rieder
   Wildlife Biologist
   EEB/HED
   Signature: Daniel Rieder 11/5/85
   Date: _____

6. APPROVED BY: Norman Cook
   Head-Section 2
   EEB/HED
   Signature: Norman Cook
   Date: 11-5-85

7. CONCLUSIONS: This study is scientifically sound.
   See Table I for reported LC_{50}'s.
   These results support registration of Affirm.

TEST MATERIAL	BINOMIAL	MOVING AVERAGE	PROBIT
MK-936 #1 ----------	0.22 ppb --	0.24 ppb ----	*
Avermectin Bla #2 ---	0.62 ppb --	0.61 ppb ----	*
Repeat Sample #2 ----	0.42 ppb --	0.47 ppb ----	*
Polar Met Sample #3 -	4.2 ppb --	21.0 ppb ----	*
Mod. Polar Sample #4 ---------	7.1 ppb --	6.3 ppb ----	*
Nonpolar Sample #5 --	25.9 ppb --	25.4 ppb ----	*
Thin Film Meta. #6 --	76.7 ppb --	76.7 ppb ----	66.5

* Since the goodness of fit probability is less than 0.05, results of the probit method are not used.

8. RECOMMENDATIONS: NA

9. BACKGROUND:

This test was performed to demonstrate the toxicity of Avermectin and its photo-degradates. Avermectin has a fairly short half-life, <24hrs in sunlight. EEB was concerned with the toxicity of the photodegradates. Daphnids were used since they were more sensitive to avermectin than the fish.

10. DISCUSSION OF INDIVIDUAL TESTS: The tests are discussed together in the following sections.

11. TEST METHODS/MATERIALS

Test Material: Avermectin (MK-936), Avermectin Bla Standard, and 4 Photo-degradates.

Percent active Ingredient: Assumed 100% a.i.
See attachment 1 for test material description.

Test Organism

Species: Daphnia magna
Acclimation: at 20°+ 1°C
Number/concentration: 20
Age/Stage: <24 hours
Source: EPA's stock culture at Duluth

Test Containers: glass

Size: 400 ml containing 300 ml water
Aerated: No
Organisms per container: 10
Replicates: 2

Test Conditions

Photoperiod: 12 hrs/day
Temperature: 20°C
Controls: Solvent Control only
Solvent: Methanol or acetone
Way test was begun: organisms added to test solution.
Measured Concentrations: No
Test Solution: Reconstituted hard water

References:

1. "Standard Method for the Examination of Water and Wastewater", 16th Edition, prepared and published jointly by APHA, AWWA, WPCF, 1985.

2. "Methods for Measuring the Acute Toxicity of Effluents to Aquatic Organisms", Environmental Monitoring and Support Laboratory - Cincinnati, Ohio, EPA-600/4-83-000, Third editions, May 1983.

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3. "Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians", National Water Quality Laboratory, EPA-660/3-75-009, April 1975.

12. REPORTED RESULTS:
See attachment 2
Table 1 48-hour LC_{50}'s summary
Raw Mortality Data
Table 2 MK-936
Table 3 Avermectin B_{1a} Standard
Table 4 Avermectin B_{1a} Standard (repeat)
Table 5 Polar and Moderately polar degradates
Table 6 Non-Polar, and Polar metobolite from thin film dish.

13. STUDY AUTHOR'S CONCLUSIONS:

Photodegradates of Avermectin are less toxic to Daphnids than parent.

14. REVIEWER DISCUSSION

a. Methods/Procedures: The procedures were acceptable. The test materials were Avermectin (MK-936), Avermectin B_{1a} and its photodegrates.

Attachment 1 for a description of the 6 test materials. Basically the photodegradate test materials were generated by exposing the parent to light either in an aqueous solution (Samples 3, 4, and 5) or as a thin film (Sample 6). Both methods of exposure produce the same degradates although in different propotions. The reported concentrations for samples 2-6 were based on radio activity and are this considered to be in ppb of 100% a.i.

The reviewer notes that samples 3 and 4 were tested with one concurrent control as were samples 5 and 6. This does not detract from the validity of the test as the controls were run on the same day as the tests they support. The controls were solvent controls.

Some of the spans between concentrations are greater than normally desired, (i.e. each concentration greater more than 60% greater than nest lower concentration) see test concentrations for samples 3, 4, 5, and 6.

b. Statistics: Independent statistics were conducted. The results are attached. (Attachment 3)

c. Discussion/Results:

The results of reviewer statistics using Stephans LC_{50} computer program, are as follows. They generally support the statistics reported.

TEST MATERIAL	BINOMIAL	MOVING AVERAGE	PROBIT
MK-936 #1 ----------	0.22 ppb --	0.24 ppb ----	*
Avermectin B_{1a} #2 ---	0.62 ppb --	0.61 ppb ----	*
Repeat Sample #2 ----	0.42 ppb --	0.47 ppb ----	*
Polar Met Sample #3 -	4.2 ppb --	21.0 ppb ----	*
Mod. Polar Sample #4 ---------	7.1 ppb --	6.3 ppb ----	*
Nonpolar Sample #5 --	25.9 ppb --	25.4 ppb ----	*
Thin Film Meta. #6 --	76.7 ppb --	76.7 ppb ----	66.5

* Since the goodness of fit probability is less than 0.05, results of the probit method are not used.

The span between concentration does not detract from the usefulness of these tests. These tests show the toxicological relationship between the various metabolites of Avermectin. Generally, the metabolites are very highly toxic to daphnids but not as toxic as the parent.

d. Adequacy: These 6 tests are scientifically sound. They fulfill the guideline requirments for acute aquatic invertebrate tests with metabolites and parent material.

15. COMPLETION OF ONE-LINER: One liner completed

16. CBI APPENDIX: N/A

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Attachment 1

Description of Test Materials

Page _____ is not included in this copy.

Pages 1 through 8 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

✓ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Attachment 2 Tables 1-6

Raw mortality data and Reported Results.

Page _____ is not included in this copy.

Pages 10 through 22 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

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Attachment 3

Reviewer Statistics

122804 AVERMECTIN - MK-936 SAMPLE 1 - DAPHNIA MAGNA LC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
1	20	19	95	2.00272E-03
.5	20	16	80	.590897
.25	20	12	60	25.1722
.15	20	5	25	2.06947
.1	20	3	15	.128841
.05	20	0	0	9.53674E-05
.025	20	0	0	9.53674E-05
.0125	20	1	5	2.00272E-03

THE BINOMIAL TEST SHOWS THAT .15 AND .5 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS .216849

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
5	.0629984	.244389	.19505	.318288

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
4	.734858	6.07845	0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED
USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 2.34779
95 PERCENT CONFIDENCE LIMITS = .335175 AND 4.36041

LC50 = .234193
95 PERCENT CONFIDENCE LIMITS = .0723611 AND 1.80344

LC10 = .0673971
95 PERCENT CONFIDENCE LIMITS = 7.09307E-05 AND .152915

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122804 AVERMECTIN - AVERMECTIN B1A SAMPLE 2 - DAPHNIA MAGNA LC50
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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
1	20	18	90	.0201225
.5	20	6	30	5.76592
.25	20	0	0	9.53674E-05
.15	20	3	15	.128841
.1	20	3	15	.128841
.05	20	1	5	2.00272E-03
.025	20	0	0	9.53674E-05
.0125	20	1	5	2.00272E-03

THE BINOMIAL TEST SHOWS THAT .25 AND 1 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS .620028

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
2	.0760279	.609065	.516037	.742589

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.980463	4.8714	0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED
USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.59608
95 PERCENT CONFIDENCE LIMITS = .0156683 AND 3.1765

LC50 = .631463

122804 AVERMECTIN - AVERMECTIN B1A SAMPLE 2 (REPEAT) DAPHNIA LC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
1	20	14	70	5.76592
.5	20	12	60	25.1722
.25	20	4	20	.590897
.15	20	3	15	.128841
.1	20	0	0	9.53674E-05
.05	20	1	5	2.00272E-03
.025	20	0	0	9.53674E-05
.0125	20	1	5	2.00272E-03

THE BINOMIAL TEST SHOWS THAT .25 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS .423532

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
2	.374194	.472116	.285819	.728122

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.649947	3.54403	1.64437E-03

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.69723
95 PERCENT CONFIDENCE LIMITS = .328935 AND 3.06552

LC50 = .543658
95 PERCENT CONFIDENCE LIMITS = .238436 AND 18.688

LC10 = .0970616
95 PERCENT CONFIDENCE LIMITS = .0010611 AND .222816

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NOTE: THERE WAS CONTROL MORTALITY, BUT AT LEAST ONE
OF THE LOWER CONCENTRATIONS HAD ZERO MORTALITY.
THEREFORE, ABBOTT'S CORRECTION IS NOT APPLICABLE.

122804 AVERMECTIN - POLAR METABOLITE SAMPLE 3 - DAPHNIA MAGNA LC50
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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
100	20	20	100	9.53674E-05
10	20	1	5	2.00272E-03
5	20	12	60	25.1722
1	20	4	20	.590897
.5	20	0	0	9.53674E-05
.3	20	0	0	9.53674E-05

THE BINOMIAL TEST SHOWS THAT 1 AND 100 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 4.18588

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
2	.279044	21.0816	10.3396	56.0744

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	1.34662	7.13779	0

A PROBABILITY OF 0 MEANS THAT IT IS LESS THAN 0.001.

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED
USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.35652
95 PERCENT CONFIDENCE LIMITS =-.217639 AND 2.93069

LC50 = 10.2629
95 PERCENT CONFIDENCE LIMITS = 0 AND +INFINITY

LC10 = 1.18865
95 PERCENT CONFIDENCE LIMITS = 0 AND 8.71067
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NOTE: BECAUSE THERE WAS CONTROL MORTALITY, AND NONE
OF THE LOWER CONCENTRATIONS PRODUCED ZERO MORTALITY,
THE DATA HAS BEEN SUBJECTED TO ABBOTT'S CORRECTION.

122804 AVERMECTIN - MOD. POLAR MET. SAMPLE 4 - DAPHNIA MAGNA LC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
100	19	19	100	1.90735E-04
10	19	14	73.6842	.960541
5	19	5	26.3158	3.17841
1	19	4	21.0526	.960541
.5	19	0	0	1.90735E-04
.3	19	3	15.7895	.221252

THE BINOMIAL TEST SHOWS THAT 1 AND 10 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 7.07107

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	.257031	6.28434	2.48171	16.0054

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.591902	3.08122	.0150918

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED
USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.33909
95 PERCENT CONFIDENCE LIMITS = .308858 AND 2.36932

LC50 = 5.1397
95 PERCENT CONFIDENCE LIMITS = 1.21526 AND 84.1138

LC10 = .578803
95 PERCENT CONFIDENCE LIMITS = 1.10776E-03 AND 2.07563

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122804 AVERMECTIN - NONPOLAR MET. SAMPLE 5 - DAPHNIA MAGNA LC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
100	20	19	95	2.00272E-03
10	20	3	15	.128841
5	20	1	5	2.00272E-03
1	20	1	5	2.00272E-03
.5	20	1	5	2.00272E-03
.3	20	0	0	9.53674E-05

THE BINOMIAL TEST SHOWS THAT 10 AND 100 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 25.9197

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
2	.0871172	25.3619	17.2541	41.2346

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	.904526	3.89955	3.60817E-03

SINCE THE PROBABILITY IS LESS THAN 0.05, RESULTS CALCULATED
USING THE PROBIT METHOD PROBABLY SHOULD NOT BE USED.

SLOPE = 1.56853
95 PERCENT CONFIDENCE LIMITS = .0767546 AND 3.0603

LC50 = 22.9291
95 PERCENT CONFIDENCE LIMITS = 3.77517 AND 2.69144E+07

LC10 = 3.55394
95 PERCENT CONFIDENCE LIMITS = 7.39678E-11 AND 15.0195

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122804 AVERMECTIN - THIN FILM MET. SAMPLE 6 - DAPHNIA MAGNA LC50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
100	20	11	55	41.1901
10	20	3	15	.128841
5	20	4	20	.590897
1	20	0	0	9.53674E-05
.5	20	0	0	9.53674E-05
.3	20	0	0	9.53674E-05

THE BINOMIAL TEST SHOWS THAT 10 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 76.6549

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
1	.547919	76.6549	32.6799	1537.85

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
4	.163366	1	.588108

SLOPE = 1.11853

95 PERCENT CONFIDENCE LIMITS = .666434 AND 1.57062

LC50 = 66.4504

95 PERCENT CONFIDENCE LIMITS = 30.9148 AND 260.512

LC10 = 4.86491

95 PERCENT CONFIDENCE LIMITS = 1.56586 AND 9.93066

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